

Research evaluation

EVALUATION REPORT OF THE UNIT
UNIS – Unité de neurobiologie des canaux
ioniques et de la synapse

UNDER THE SUPERVISION OF THE
FOLLOWING ESTABLISHMENTS AND
ORGANISMS:

Aix-Marseille Université
Inserm

EVALUATION CAMPAIGN 2022-2023
GROUP C

Rapport publié le 22/12/2023



In the name of the expert committee¹:

Mr. Vania BROCCOLI

For the Hcéres²:

Mr. Stéphane Le Boulter, acting president

Under the decree n° 2021-1536 of 29th November 2021:

¹ The evaluation reports "are signed by the chairperson of the expert committee". (Article 11, paragraph 2);

² The president of the Hcéres "countersigns the evaluation reports established by the expert committee and signed by their chairperson." (Article 8, paragraph 5).

This report is the result of the unit's evaluation by the expert committee, the composition of which is specified below. The appreciations it contains are the expression of the independent and collegial deliberation of this committee. The numbers in this report are the certified exact data extracted from the deposited files by the supervising body on behalf of the unit.

MEMBERS OF THE EXPERT COMMITTEE

Chairperson: Mr. Vania BROCCOLI, San Raffaele Scientific Institute, Milan, Italie.

Mr. Denis JABAUDON, Université de Genève, Suisse.

Mr. Bruno LAPIED, Université d'Angers, (Representative of CNU 69).

Experts :

Ms. Daniela POPA CARREL, Inserm, Paris, (Representative of Inserm CSS4).

Mr. Orestis FAKLARIS, CNRS, Montpellier, (Representative of supporting personnel).

HCÉRES REPRESENTATIVE

Ms. Nadia SOUSSI-YANICOSTAS

CHARACTERISATION OF THE UNIT

- Name: Unité de neurobiologie des canaux ioniques et de la synapse
- Acronym: UNIS
- Label and number: inserm – AMU UMR1072
- Composition of the executive team: Dominique DEBANNE

SCIENTIFIC PANELS OF THE UNIT

SVE5: Neurosciences

THEMES OF THE UNIT

The main scientific focus of UNIS is the investigation of the biology and physiology of ion channels and dynamics of synaptic plasticity in health and disease. Through a range of methodologies from molecular modelling, electrophysiological techniques, pharmacology and network analysis, the unit investigates the mechanisms underlying the regulation of neuronal excitability and synaptic communication. UNIS also has long-standing interests on LG1-dependent mechanisms regulating excitability/epilepsy and molecular mechanisms of the botulinum neurotoxins. A recent focus of the unit is the molecular modelling and infection mechanisms of the different variants of SARS-CoV2.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

UNIS is currently a single team unit directed by Dr. Dominique Debanne. In the previous contract (2012–2017), UNIS was a multi-team unit organised in three independent research teams. However, two of these teams were closed by inserm in 2017. Consequently, today UNIS is organised into a single team with three thematic axes (TAs). Furthermore, besides UNIS, a team emerges from the Centre de Recherche en Neurobiologie-Neurophysiologie de Marseille (LNC).

UNIS is currently located at the North Campus in Marseille. However, a new location has been identified at the Luminy Campus in the inserm TPR2 building that is already hosting three other institutes: TAGC (Theories and Approaches of Genomic Complexity, inserm-AMU UMR1090 at TPR2), LAI (Adhesion and Inflammation Lab Unit) and AA (Arthrite Autoimmunes Unit, inserm-AMU UMR1097 at TPR2).

RESEARCH ENVIRONMENT OF THE UNIT

UNIS is a founding member of NeuroMarseille, a thematic Institute funded by the Programme d'Investissement d'Avenir (PIA) which gathers the nine neuroscience research units in the city since 2020 for common scientific initiatives and science training. UNIS is embedded in a stimulating environment although the institutions are located at distant locations throughout the city as it is on the North Campus. At the present time in the North Campus UNIS shares the animal husbandry and imaging equipment with a CNRS group at Laboratoire de Neurosciences Cognitives (LNC). Moving to the Luminy Campus, UNIS will benefit from the support of six technicians shared with the other inserm units within the same TPR2 building. The UNIS will join the Turing Centre for Living System (CenTuri) a thematic Institute of Convergence between Biology and Mathematics, funded by the PIA and AMiDEX, which grants positions for young scientists. UNIS is affiliated with two Région SUD-inserm's doctoral programs and a 'Région SUD' grant. UNIS has well-developed collaborations with local and national groups in a wide range of multidisciplinary expertise from molecular modelling, mathematicians, pathologists, and developmental biologists. At the International level, UNIS has some solid collaborations testified by collaborative publications. UNIS hosted an ERC-consolidator funded team leader, who has left UNIS in 2021. The Unit has established collaborative actions with National (IPSEN, Sanofi & Axorus) and European (UCB Pharma) companies that have granted an economical return (about 86 K€).

UNIT WORKFORCE: in physical persons at 31/12/2021

Permanent personnel in active employment	
Professors and associate professors	2
Lecturer and associate lecturer	1
Senior scientist (Directeur de recherche, DR) and associate	2
Scientist (Chargé de recherche, CR) and associate	2
Other scientists (Chercheurs des EPIC et autres organismes, fondations ou entreprises privées)	0
Research supporting personnel (PAR)	10
Subtotal permanent personnel in active employment	17
Non-permanent teacher researchers, researchers and associates	3
Non-permanent research supporting personnel (PAR)	0
Post-docs	0
PhD Students	6
Subtotal non-permanent personnel	9
Total	26

DISTRIBUTION OF THE UNIT'S PERMANENTS BY EMPLOYER: NON-TUTORSHIP EMPLOYERS ARE GROUPED UNDER THE HEADING 'OTHERS'.

Employer	EC	C	PAR
Inserm	0	2	8
Aix-Marseille Université	3	0	2
CNRS	0	2	0
Total	3	4	10

UNIT BUDGET

Recurrent budget excluding wage bill allocated by parent institutions (total over 6 years)	1227
Own resources obtained from Regional calls for projects (total over 6 years of sums obtained from AAP idex, i-site, CPER, territorial authorities, etc.)	61
Own resources obtained from National calls for projects (total over 6 years of sums obtained on AAP ONR, PIA, ANR, FRM, INCa, etc.)	1277
Own resources obtained from International call for projects (total over 6 years of sums obtained)	1597
Own resources issued from the valorisation, transfer and industrial collaboration (total amount obtained over 6 years through contracts, patents, service activities, services, etc.)	86
Total in k€	4,248

GLOBAL ASSESSMENT

UNIS is a renowned scientific centre for ion channel biology, synaptic plasticity and pathological mechanisms in epilepsy. In the reference period, the UNIS scientific production has been excellent with some of the studies published in high-profile journals with wide visibility (1 Sci. Adv., 2 Brain and 6 PNAS). These studies are generally original and innovative confirming the high level of expertise and visibility of UNIS in these scientific fields. UNIS is organised in three thematic axes (TAs) and most of the achievements are related to the activities of two of the TAs. The third TA has not performed at the same level in terms of scientific achievements and the principal investigator left UNIS in 2021. The unit has been excellent in attracting research funding at the Regional (2 Région SUD grants, 1 AMiDEX, 2 FRM doctoral grants, 2 NeuroMarseille) and National (1 FRM Equipe, 3 ANR grants, 1 Fondation de France) levels. However, the Institute has to implement strategic actions to affiliate with International consortia and attract intra or extra-European research funding. The relative small size of the unit has not prevented from reaching excellent results in scientific production and quality of research in this period. However, this size might condition the future development of the unit both in terms of timely acquisition of new technological expertise or approaching new research initiatives. UNIS will relocate at the Inserm TPR2 building at the Luminy Campus in 2023 sharing some infrastructure with three other units. However, UNIS should find opportunities to partner or integrate with other neuroscience research institutions present in the campus. This partnership might become an important cornerstone for UNIS to leverage on its profound expertise for building opportunities for novel collaborative initiatives, increasing the sharing of additional core facilities and facilitating technological developments.

DETAILED EVALUATION OF THE UNIT

A – CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

The first recommendation of the previous HCERES committee was to pursue the development of cell imaging advanced technologies in the unit. To respond to this request, they have recruited a Research Engineer in optics and a researcher with a solid experience in imaging which was instrumental to finalise the studies centred on advanced live cell imaging approaches with the development of optogenetics and optically activated reporters. Regarding the second recommendation of the previous HCERES committee asking to increase the amount of research grants, the number of grants in the period 2017–2021 has increased to twelve (1 FRM Equipe, 3 ANR grants, 1 Fondation de France, 2 Région SUD grants, 1 AMiDEX, 2 FRM doctoral grants, 2 NeuroMarseille, ...). Following the third recommendation of the previous HCERES committee to recruit postdocs on grants, UNIS has recruited five postdoctoral scientists with an international research experience and two European students. About the fourth recommendation of the previous HCERES committee to reinforce the collaboration within the unit, UNIS has continued to promote collaboration between the internal thematic axes (TA1, D. Debanne; TA2, O El Far; TA3, J.M. Gaillard) finalised by five papers (TA1 and TA2), one paper (TA2 and TA3) and one paper (TA1 and TA3). Following the fifth recommendation of the previous HCERES committee to recruit a junior professor, the unit has identified a junior professor who has applied to the Chaire de Professeur Junior in 2022.

B – EVALUATION AREAS

EVALUATION AREA 1: PROFILE, RESOURCES AND ORGANISATION OF THE UNIT

Assessment on the unit's resources

UNIS is currently a single team unit with three thematic axes. UNIS currently includes seventeen permanent staff (2 professors, 1 lecturer, four scientists and 10 technical staff), three postdocs and six doctorate students for an overall proportion between fixed-term and permanent personnel of 0.53. Fifty percent of the efforts of the UNIS members are devoted to research activity while the rest is split between teaching charges, research supervision and research administration. Financial resources of UNIS are provided by a recurrent funding from Inserm and AMU for 1227 K€, research grant funding for 3,021 k€ and 86 k€ from Industrial collaborations. Hence, UNIS has shown a strong capacity to attract academic funding to finance its own research. In accordance with its scientific goals, UNIS is equipped with eight patch-clamp rigs, three confocal microscopes with one coupled to a patch-clamp set-up, biochemistry and molecular biology facilities. Imaging instrumentation is managed by an expert engineer in optics assisted by a researcher with solid experience in imaging. An animal facility is shared with Laboratoire de Neurosciences Cognitives (LNC) at the North Campus in the current time together with a proteomic platform. Finally, they have access to commercial software for multi-scale electrophysiological analyses and neuronal modelling.

Assessment on the scientific objectives of the unit

The main scientific goal of UNIS is to understand the role of ion channels in neuronal communication, neuron network plasticity and brain diseases. The understanding of basic cellular and molecular mechanisms controlling neuronal excitability and synapse plasticity are fundamental to extract biological principles at the basis of sensory processing, memory consolidation and cognitive performance. Scientists at UNIS have provided excellent insights on the regulation and dynamics of ion channel functions during homeostatic changes in intrinsic excitability and synaptic transmission as remarked by the quality of the related publications. Through a combination of multidimensional and functional analyses of neuronal activity and synaptic processing, the unit has been able to define new roles of K⁺ and Na⁺ ion channels in shaping neuronal activity during neuronal synchronisation and synaptic plasticity. UNIS has also provided an important contribution in understanding the pathological basis of the LG1-dependent dominant epileptic disease and the detrimental effects of LG1 autoantibodies in limbic encephalitis.

Assessment on the Functioning of the unit

UNIS is a single-team unit and consequently its reduced size should facilitate the communication between the three thematic axes and their members. A steering committee is in place with the heads of the thematic axes and is organized on a monthly basis. A Laboratory Council is held once a year to validate the internal rules of procedure. Each thematic axis organises weekly scientific meetings. UNIS has appointed an *Assistant Prévention* to oversight health and safety issues and a *Personne Compétente en Radioprotection*. Each new laboratory member (usually students or postdocs) receives the *internal rules of procedure* from the responsible for Common Services and they sign an agreement of confidentiality. Finally, an inserm correspondent for the professional gender equality has been appointed by UNIS in 2021.

1/ The unit has resources that are suited to its activity profile and research environment

Strengths and possibilities linked to the context

According to the deep expertise in advance functional neuroscience, UNIS is equipped with several patch-clamp suites and three confocal microscopes. The unit has received a grant in 2022 to finance an ultra-fast two-photon microscope for advanced cell imaging of common use among the three TAs. The unit has direct access to a mouse facility in sharing with LNC at the Campus Nord. UNIS has well-trained personnel in electrophysiological recordings and optics with senior researchers supervising the technical development of these methodologies. The unit has successfully exploited proteomics for its studies establishing a strategic collaboration with the technical platform 'Plateforme Interactome NeuroTimone' (PINT). The technical staff with high-level expertise is currently at the head of the unit's facilities, defining the facility policy (e.g. equipment acquisition, writing of funding projects) in close communication with the unit director.

Weaknesses and risks linked to the context

The size of the unit is relatively small, raising more difficulties to expand the research activities and implement novel technologies. As such, the unit faces operative and logistic hurdles that require external supports. Some future developments of the unit are likely to be the integration of their functional studies with *in vivo* models and during animal behavioural tasks. These developments will likely require new expertise in 2-photon imaging, behavioural neuroscience and system neuroscience. The relative number of fixed-term researchers is relatively low respectively to the total number of permanent positions (0.53). The animal facility is suffering from a turnover of technical staff since the depart of the inserm zootechnician.

2/ The unit has set itself scientific objectives, including the forward-looking aspect of its policy

Strengths and possibilities linked to the context

The unit has finalised high-quality studies on the mechanisms regulated by ion channels that modulate intrinsic excitability and synaptic plasticity confirmed by publications in prominent journals (Zbili et al., *Sci Adv* 2020; Zbili et al., *PNAS* 2021; Ho et al., *PNAS* 2021; Fékété et al., *PNAS* 2021). These results place the unit at the forefront of this research and it is internationally renowned for its expertise and knowledge on this scientific field as proven by the number of citations of these studies (>1100 in the period 2016–2021). Given its solid and renowned expertise, the unit has established strategic collaborations for fully exploiting the implications of their studies for molecular modelling, neuronal synchronisation and brain dysfunctions that led to publications in high-quality journals (Inglebert et al., *PNAS* 2020, Zbili et al., *PNAS* 2021, Rama et al., *Sci Rep* 2017, Huang et al., *eLife* 2018, *Brain* 2020).

Weaknesses and risks linked to the context

Even if the research axis 2 has recently published relevant findings on the molecular mechanisms underlying the LG1-dependent epileptic phenotype, the future development of these studies is less clear as are its implications for the development of new models or translational implications for the disease. Since the departure of the scientific leader of the TA 3 in 2021, this branch of the unit is not fully registered in terms of scientific interests, offerent personnel and leadership.

3/ The functioning of the unit complies with the regulations on human resources management, safety, the environment and the protection of scientific assets

Strengths and possibilities linked to the context

UNIS has implemented procedures to oversight health issues and safety in the laboratory, use of radioactive material and general training of the new lab members. Gender equality policy has been followed during the recruitment of permanent and fixed-term research personnel, internal mobility, and career promotions. Health and psychological follow-ups were provided by the directorship during the lockdown period for the COVID emergency.

Weaknesses and risks linked to the context

It is not well specified in the report which actions are implemented to protect the intellectual property of the scientific discoveries made by UNIS and how these new knowledge is valorised in the private biomedical sector. UNIS has some ongoing collaborations with companies, but the exact terms of these interactions have not been fully exemplified in the report. The actions that are in place to strengthen connections with the private sector are not specified.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

UNIS is a renowned centre for basic research on ion channels and their mechanisms in controlling neuronal and synaptic plasticity. The unit has provided important and original findings that have illuminated new functions of ion channels in modulating neuronal activity, synchronisation and plasticity in health and disease states. UNIS has a good network of collaborators predominately within the country with complementary expertise that enriches the breath of its research. However, because the UNIS has too few, albeit good facilities, the unit is obliged to seek external collaborators to carry out crucial research activities for its research, as, for instance, proteomics. UNIS has obtained good funding from National agencies, but far less from International and European institutions. This is reflected by the absence of UNIS from consolidated and well-structured European research consortia funded by EU initiatives.

1/ The unit has an attractive scientific reputation and contributes to the construction of the European research area

Strengths and possibilities linked to the context

UNIS is internationally recognised for its basic studies focused on the interplay between ion channels, neuronal functions and synaptic plasticity. During the reference period, UNIS members were invited to eleven international and >5 national conferences and seminars (>5) and the Institute organised three International conferences attracting prestigious international experts at the highest scientific level. UNIS has developed advanced and competitive optogenetic and electrophysiological methodologies for studying axonal functions combining electrophysiological recordings with high-quality imaging and mathematical modelling. Some of the researchers have editorial responsibilities (Scientific Reports, Frontiers in Cellular Neuroscience and Cells) and are reviewers for a wide range of renowned scientific journals (Nature, Nature Neuroscience, Neuron, Nature Communications, Brain, PNAS). UNIS has a highly scientific reputation and attractiveness for studies on the ion channel biology.

Weaknesses and risks linked to the context

UNIS is a single-team unit with a strong focus on ion channel functions in neuronal homeostasis. Its small size might complicate the timely acquisition of new technologies and development of new research activities. UNIS will likely benefit to raise its critical mass by integrating additional scientists or merging with other teams/units with complementary expertise in the fields for instances of in vivo neuronal recording, imaging and optogenetics, mouse behaviour and neurological disorders.

2/ The unit is attractive for the quality of its staff hosting policy

Strengths and possibilities linked to the context

UNIS provides good working conditions for early career scientists providing them with their own space and computers. Scientific mentorship is provided with regular discussion about experimental data at lab meetings with weekly frequency and the possibility to present their own results at the plenary meetings of the institute. Most PhD students (12 out of 13) and all postdocs (8 out of 8) have publications in competitive journals confirming the quality and significance of the research projects in which they have carried out and the capacity of their mentors.

Weaknesses and risks linked to the context

UNIS seems to have faced some difficulties in obtaining permanent positions for their early career researchers. In fact, the few applications for inserm tenure positions were not successful. This raises some concerns about the turnover of the scientific personnel for unit with such a small size.

3/ The unit is attractive because of the recognition gained through its success in competitive calls for projects

Strengths and possibilities linked to the context

In the period under scrutiny, UNIS members obtained grants from ANR (5), Equipe FRM (1), Fondation de France (1), Région-Sud (doctoral). This grant funding enabled the recruitment of eight postdocs, nine doctorate students and four technicians. These achievements strongly indicate the high-quality and competitive hedge of the research performed at UNIS.

Weaknesses and risks linked to the context

UNIS hosted an ERC Consolidator PI, who left the Institute in 2021. In the reference period, UNIS has not attracted any other European and International funding. The report does not specify how many applications were finalised for International grant calls with a negative response. UNIS has multiple collaborations with International scientists that led to a few jointed publications but they are not sufficient to establish well structured and competitive international consortia for obtaining EU funds.

4/ The unit is attractive for the quality of its major equipment and technological skills

Strengths and possibilities linked to the context

UNIS is well equipped for electrophysiological recordings (8 patch-clamp rigs) and confocal imaging (LSM780 & LSM710 microscopes) covering the present research needs of the unit. UNIS confocal microscopy facility is oversight by an engineer with expertise in optics and supervised by a scientist with solid experience in imaging. UNIS runs a facility for biochemistry with a surface plasmonic resonance apparatus for advanced biomolecular interaction analysis with expert supervision and hands-on training.

Weaknesses and risks linked to the context

The equipment hold by UNIS is adequate for its current research which is mostly on in vitro models, but not for in vivo microscopy and recordings. This next step is demanding and can hardly be efficiently developed by a single team and, thus, is calling for integrating new scientific personnel or integrating with other teams with complementary expertise.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The scientific production of the unit is of excellent quality, providing important advances in the basic understanding of ion channels in modulating neuronal intrinsic functions and synaptic plasticity during different physiological processes and disease conditions. The relevance of its work is confirmed by publications in high-quality peer-reviewed journals (PNAS, Sci. Adv., Brain) and with a good citation record (>1100 citations in the period 2016–2021). All UNIS members have contributed to the scientific production of the unit and most early career researchers have publications as first authors confirming the good training in place in the unit. The team went through an important reorganisation, but this did not affect significantly the scientific production; most of this production is under the direct supervision of the director of the team (TA1) and significantly less from the TA2 and 3. It is also noteworthy the interesting results obtained with the molecular studies on SARS-CoV2 by the UNIS members that produced a significant number of publications in a very short timeframe (5 original publications cited > 370 times since 2020).

1/ The scientific production of the unit meets quality criteria

Strengths and possibilities linked to the context

Between 2016 and 2021, UNIS produced 70 peer-reviewed publications. Forty-two were original publications, two were clinical articles and sixteen were reviews. The overall quality of the scientific production is excellent with a good fraction of papers (n=9) published in top quality journals (PNAS, Brain and Sci. Adv.) The high value of these publications is also confirmed by the high number of citations (>1100 over the 2016–2021 period). UNIS has provided new fundamental knowledge on the functions of ion channels in controlling neuronal activity and plasticity in health and disease. Importantly, most of the research personnel included tenured scientists, early career researchers and technicians are co-authors in one or several publications. However, most of the scientific production of the UNIS is under the direct supervision of the director of the team (TA1) and less from the TA2 and 3. Most PhD and postdocs have at least one first author publication confirming the high productivity of the unit and its ability to successfully train young researchers.

Weaknesses and risks linked to the context

The TA3 has performed less well respectively to the other two TAs. In fact, both the number of original papers (*J Neurosci* 2012; *eLife* 2014; *J Neurosci* 2019) and their overall quality are not comparable with those produced by the other two TAs. This TA is no longer part of the UNIS as the team went through a reorganisation with the departure of several researchers and the arrival of new ones.

2/ Scientific production is proportionate to the research potential of the unit and shared out between its personnel

Strengths and possibilities linked to the context

The number of articles (70) produced by UNIS can be considered adequate for its staff number (~30 persons with ~8/10 postdocs & PhD students). It is to be highlighted that the high-quality and novelty of some of these publications discovering new properties of ion channels and their neuronal network mechanisms is much more preferable to the counting of the number of publications.

Weaknesses and risks linked to the context

Overall, no weaknesses were identified related with this aspect.

3/ The scientific production of the unit complies with the principles of research integrity, ethics, and open science

Strengths and possibilities linked to the context

Prior to publication, experimental works are presented and thoroughly discussed in group or lab meetings within UNIS and with the director, Mr. Dominique Debanne. Most unpublished data are presented in National and International meetings under the form of posters where they are discussed with peers. All PhD students undergo specific training on scientific integrity. Experimental procedures with animals at UNIS have been approved by specific APAFIS authorisations. To favour open science most of the original articles of UNIS have been preliminarily deposited in an open archive (BioRxiv or research square).

Weaknesses and risks linked to the context

It is not detailed if the unit provides laboratory books with either numbered pages or the electronic LabCollector. It is not specified which databases and archives are used for storage and sharing of databases and original datasets related to published work.

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

Assessment on the inclusion of the unit's research in society

UNIS has developed partnerships with several companies indicating its attention in looking for synergies with the private sector and raising income by valorising its research products and technical expertise. Its expertise in molecular modelling has been valorised by setting up close synergies with the private sector. In addition, the unit has developed a paid service for screening ion channel autoantibodies in patient sera for clinical care. Given the relative small size of the unit and its main focus on basic research, these initiatives confirm its proactive effort to develop synergies with the private sector. Two start-ups were created during the last five years. The unit has finalised only one patent application and the important expertise in electrophysiology are not further valorised with commercial partnerships,

1/ The unit stands out by the quality of its non-academic interactions

Strengths and possibilities linked to the context

UNIS has developed partnership contracts with several industrial companies, in particular: Two doctoral grants for three years have been obtained with the company CILOA in the frame of the Région-SUD calls for studying protein native conformation in exosomes. A contract from IPSEN innovation for detecting enzymatic activity (61 k€). The unit provides primary antibodies to Sanofi, IPSEN Pharma and Institut Pasteur (respectively for 11.5 k€, 9.5 k€ and 3.5 k€). The unit established a partnership with Neuroservice (Aix-en-Provence) which obtained an AMiDEX Pépinière d'Excellence grant (25 k€) and a collaborative project with Axorus (Lille) to test the incidence of neuronal stimulation with artificial retinas on neuronal firing properties. UNIS offers paid activities for the detection of anti-ion-channel antibodies in patient sera for hospitals (157.4 k€). Over the last five years, the unit played a key role for the creation of two start-up companies (AmyPore and BM2S). These initiatives indicate that UNIS actively developed synergies with the private sector through the valorisation of the unit's research products

and expertise, that contribute to raising funding, provide doctoral grants and stay in close contact with the non-academic world.

Weaknesses and risks linked to the context

The overall income obtained by the partnerships with the private sector and sales of products is still relatively low in respect to the overall annual budget of the unit.

2/ The unit develops products for the socio-economic world

Strengths and possibilities linked to the context

As detailed above, UNIS has partnerships with biotech companies and sells antibodies to academic and private institutions. It also increases its revenue by performing screenings in patient sera for anti-ion-channel antibodies.

Weaknesses and risks linked to the context

UNIS has a strong expertise in electrophysiology that could be further valorised through partnerships with private companies. UNIS has finalised one patent application in the field of improving protein molecular modelling using exosomes and there is marge for more patent applications for the unit. The unit could work more closely with the expertise valorisation through inserm valorisation and SATT structures.

3/ The unit shares its knowledge with the general public and takes part in debates in society

Strengths and possibilities linked to the context

Outreaching activities by UNIS are concentrated during the 'Brain Week' (semaine du cerveau) that takes place each year in March. PhD students visit schools in Marseille and the Bouches-du-Rhône department to promote neurobiology research and arouse vocations. Moreover, on the occasion of some of the unit's scientific publications, UNIS created and provided online articles and videos that help dissemination of the results.

Weaknesses and risks linked to the context

Dissemination activities by UNIS are mainly concentrated in the annual 'Brain Week' and carried out by the PhD students. UNIS seems to have not developed outreaching activities in collaboration with other research units in the campus. UNIS members have not been involved in public seminars and events for scientific dissemination (like for instance 'Fête de la Science'). UNIS website is not rich of contents and is limited to the unit's main research axes, with no references to updated activities or related events.

C - RECOMMENDATIONS TO THE UNIT

Recommendations regarding the Evaluation Area 1: Profile, resources and organisation of the unit

The unit is a single team structure, which, then, facilitates the practical organisation and interaction between the different supervising bodies. The unit has an excellent performance in terms of scientific production and a very good attractiveness despite the critical mass of the unit is rather small. Hence, this compact size has not prevented the excellent results obtained in the period of reference but raises concerns for the future development of the unit in terms of rapid development of new technologies and its long-term competitive advantages. It is also notable that the thematic carried out regarding protein aggregate toxicity in neurodegenerative diseases are less aligned with the main interests of the UNIS in terms of both scientific questions and technical development. This thematic would benefit to build strong internal synergies with cellular and molecular experts in models of neurodegenerative disorders and therapeutics in vivo delivery. Finally, the collaboration with the clinicians of the CHU-Nord Ophthalmology unit has been limited to some technical support for one specific project. It has not been clarified how this interaction is going to be developed in the future for a deeper involvement in the research projects and integration within the Institute.

UNIS is going to relocate in the TPR2 building in 2023 sharing infrastructure with other three inserm units with other scientific interests. Thus, a strategic choice might be to develop strong scientific and operative synergies with INMED, a leading Institute in Neuroscience located in the same Campus. These new synergies will provide UNIS with the access and partnership on other technological and scientific domains, on one side, and, on the other

side, to develop more collaborative projects exploiting its outstanding expertise in ion channels biology in other scientific contexts.

The relative ratio between hired scientist and permanent personnel is relatively low (0.53). To improve this parameter, it would be helpful to attract more research funding exploring new opportunities. UNIS has shown an excellent performance in obtaining Regional and National research grants. However, UNIS should put in place strategic initiatives to obtain funding from European and International agencies. UNIS should develop a strategy for its facilities in the new Campus and think of their partial fusion with the existing ones. This could help to ask for permanent positions (i.e. zootechnician). As a result, the unit should decide on the billing policy of its facilities in the new Campus and their governance.

Recommendations regarding the Evaluation Area 2: Attractiveness

UNIS is certainly an internationally renowned centre for studies on the ion channel biology, which has provided innovative and original findings in this field of neuroscience. Thus, its scientific expertise and results are providing a high level of international recognition in the field. Another aspect of this is the ability of UNIS to recruit young scientists from abroad with already good skills and scientific knowledge. To further expand the scientific stature of UNIS, it would be strategic to develop more synergies with international centres and participate to well-structured European consortia and initiatives to also acquire international funding that has been missing up to now.

Recommendations regarding Evaluation Area 3: Scientific Production

UNIS is very well recognised for its expertise in the field of ion channel biology and neuronal plasticity. It has made important contributions towards a better understanding of the mechanistic role of ion channels in controlling axonal excitability and synaptic homoeostasis in health and disease. Some of these studies are reported in highly visible publications in highly visible journals with a relevant number of citations. The unit has also successfully continued their investigations on LGII dysfunctions in epilepsy and the mechanisms of trafficking of the botulinum neurotoxin receptor. This scientific work is highly original and innovative, but it is going to stop and not continued in the future.

Recommendations regarding Evaluation Area 4: Contribution of Research Activities to Society

UNIS has developed new collaborations with companies and hospitals for obtaining funding through the sharing of its internally developed reagents or providing services. However, the income for these activities is relatively low. On this respect, the activities related to molecular modelling and structural biology are well appreciated since they have led to important partnerships with private companies and the initial establishment of a new start-up. However, these activities can be further strengthened in order to expand this collaborative network. The engagement for science public outreach is mainly concentrated on the yearly 'Brain Week'. UNIS should dedicate more efforts to find additional opportunities to share its scientific knowledge with the public. UNIS can likely become a driving actor in more initiatives, such as the development of partnerships with other institutes, as for instance INMED.

CONDUCT OF THE INTERVIEWS

Date(s)

Start:	December 1 st , 2022, at 8:30 am
End:	December 1 st , 2022, at 6:30 pm
8:30 a.m.-8:45 a.m.	Closed session with the committee
8:45 a.m.-9 a.m.	Presentation of the committee
9 a.m.-9:45	Presentation of the unit by the director Mr. D. DEBANNE, (30 min presentation + 15 min discussion with the committee)
9:45-10:55	Results and projects: (Mr. D. DEBANNE) (40 min presentation + 20 min questions + 10 min in private PI-committee); Neuronal communication (Mr. D. DEBANNE, 10 min presentation); Plasticity (Mr. D. DEBANNE, Mr. P. MARCAGGI & Mr. M. RUSSIER, 20 min presentation); Brain diseases (Mr. M. RUSSIER & Mr. J. FANTINI, 10 min presentation)
10:55-11:10	Coffee break
11:10-11:25	Research group project: Background GABAergic activity in hippocampal function and disease (Ms. K. Nasrallah) (10 min presentation + 5 min questions)
11:25-11:50 1 p.m.	Meeting with engineers, technicians and administrative personnel in French 11:50-Private meeting of the visiting committee (report preparation)
1 p.m.-2 p.m.	Lunch
2 p.m.-2:30 p.m.	Meeting with students and postdocs
2:30 p.m.-3 p.m.	Meeting with scientists, no lab director
3 p.m.-3:40 p.m.	Discussion with the director Mr. Dominique DEBANNE
3:40 p.m.-4:10 p.m.	Discussion with the representative of the funding bodies
4:10 p.m.-6 p.m.	Private meeting of the visiting committee (report preparation, closed-door)
6 p.m.	End of the visit

Interview conducted: online

INTERVIEW SCHEDULE

PARTICULAR POINT TO BE MENTIONNED

GENERAL OBSERVATIONS OF THE SUPERVISORS

Le Président de l'université

au

Département d'Évaluation de la recherche -
Hcéres

Objet : Observations de l'unité relatives au
rapport d'évaluation des experts Hcéres

N/Réf. : VPR/LS/AMS/CM – 23-07

Dossier suivi par : Cécile Merle

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Vos réf :

DER-PUR230023373 - UNIS - Unité de neurobiologie des canaux ioniques et de la synapse

Marseille, le mardi 25 juillet 2023

Madame, Monsieur,

Je fais suite au mail que vous nous avez adressé le 06/07/2023 dans lequel vous me communiquez le rapport d'évaluation Hcéres de l'Unité UNIS - Unité de neurobiologie des canaux ioniques et de la synapse.

Comme demandé dans ledit mail, je vous fais part des observations de portée générale émises par l'unité:

Nous remercions vivement l'ensemble des membres du comité HCERES pour ses commentaires très positifs et ses suggestions constructives.

Recommandations sur le critère d'évaluation 1 : profile, ressources et organisation de l'unité

L'unité a été jugée **très performante** en termes de **production scientifique** et **attractivité**. Elle va se relocaliser sur le campus de Luminy et permettra non seulement de **renforcer la dynamique** de site mais pourra également **bénéficier** d'un **environnement scientifique de qualité**, des moyens apportés par **l'Institut de Convergence** Mathématiques / Biologie (**CenTuri**) et participer d'une **synergie** avec les autres unités de biologie du campus. Une interrogation émise par le comité HCERES concerne la taille relativement modeste de l'unité qui pourrait limiter le développement de nouvelles techniques expérimentales. Plusieurs stratégies sont déjà déployées pour corriger cela. Tout d'abord, les effectifs du prochain contrat quinquennal vont augmenter de >70% avec 1) l'obtention, cette année, de contrats de recherche (3 A*Midex, 1 ANR, et 1 FRC...) permettant le recrutement d'au moins 3 postdocs et 2 doctorants, 2) le recrutement d'au moins 2 jeunes chercheuses de talent (Coralie Di Scala et Kaoutsar Nasrallah) qui vont obtenir des contrats de recherche nationaux et internationaux afin de recruter des jeunes chercheurs et d'augmenter ainsi les effectifs de l'unité et 3) l'intégration d'une partie du service d'ophtalmologie du CHU Nord (9 personnes). Le recrutement de K Nasrallah sur une chaire d'excellence A*Midex est en phase finale (CDS prévu à l'automne) et C Di Scala a déjà été sélectionnée à l'oral CR-INSERM et elle candidate également sur une chaire d'excellence INSERM. Leur recrutement permettra également de mettre en place de nouveaux outils comme les injections virales (AAV ; K Nasrallah), l'exploration comportementale (K Nasrallah et C Di Scala), la photométrie *in vivo* (K Nasrallah) ainsi que le suivi de particule unique (C Di Scala).

Parallèlement, le développement de nos collaborations internationales (Europe, Chine et USA) et nationales nous permettra de développer de nouvelles techniques pour 1) identifier les

conditions de la libération de la somatostatine par les interneurons en utilisant des outils originaux (senseurs de somatostatine fluorescent en collaboration avec Y Li – Beijing Chine et G Sandoz, Nice France), 2) comprendre les liens entre la sclérose en plaque et l'épilepsie (collaboration en développement avec P Chauvel, Pittsburgh USA et F Wendling, Rennes France) et 3) mettre en place de nouvelles thérapies contre l'épilepsie (collaboration avec S Stupp, Chicago USA).

Enfin, nous lançons un appel d'offre pour identifier un(e) jeune chercheur(e) de haut niveau et spécialisé(e) dans la neurophysiologie et l'imagerie *in vivo*. Ainsi, l'UNIS sera encore plus armée pour affronter les nouveaux défis technologiques et conceptuels en neurosciences.

Par ailleurs, nous avons déjà largement prouvé que la taille de l'unité ne prévalait pas des résultats en termes de nombre de publications à haut facteur d'impact (1 Science Advances, 2 Brain, 7 PNAS, 1 eLife, etc...), en termes de dynamisme et de créativité permettant l'obtention de contrats de recherche compétitifs (4 A*Midex, 5 ANR, 2 FRM, FRC, ...).

La seconde recommandation concerne le renforcement des études sur les interactions protéines-lipides dans les maladies neurodégénératives. Comme suggéré par le comité, nous allons 1) nous rapprocher d'experts des maladies neurodégénératives¹ pour mieux appréhender ces questions et améliorer l'application thérapeutique du peptide amyloïde, et 2) renforcer les collaborations internes afin que cette thématique s'appuie davantage sur l'expertise du laboratoire en électrophysiologie.

La troisième recommandation concerne le renforcement de l'implication des ophtalmologistes du CHU Nord dans les projets de l'unité. Le **projet portant sur l'amblyopie** initialement entamé en collaboration avec le service du Professeur D Denis a été **considérablement étendu** ces derniers temps par une **approche moléculaire** (spectrométrie de masse, patch-seq, proximity ligation assay, etc...) soutenue par un contrat de recherche FRC. De plus, nous avons récemment identifié **2 praticiens hospitaliers** (Dr A Aziz et Dr P Ramtohol) du service d'ophtalmologie du CHU Nord qui **débutent une thèse de Doctorat en neurosciences** en septembre 2023 **dans l'unité** pour étudier les mécanismes cellulaires et moléculaires de l'amblyopie dans le dLGN (Dr A Aziz) et la rétine (Dr P Ramtohol). Ainsi, l'intégration des membres du service d'ophtalmologie à l'UNIS est donc considérablement renforcée et clarifiée au-delà du support technique initialement entrepris pour réaliser les sutures de paupières et les injections intraoculaires de traceurs.

La quatrième recommandation concerne la possibilité d'attirer plus de fonds internationaux. Nous comptons diversifier les fonds obtenus par l'unité en étant plus actifs dans nos réponses aux appels d'offre internationaux (ERC, EraNet, Marie Skłodowska-Curie, EMBO, HFSP, NIH, etc...). En particulier, C Di Scala et K Nasrallah vont déposer un contrat EraNet prochainement. D Debanne projette de faire une demande d'ERC Synergy en partenariat avec G Sandoz (IbV, Nice). K Nasrallah envisage de répondre aux appels à projets de la fondation CURE Epilepsy. S Incontro va demander un contrat HFSP et un contrat NIH en collaboration avec le laboratoire de S Stupp. P Marcaggi et M Russier envisagent de déposer un contrat EMBO en partenariat avec A Hierlemann et JJ Garrido. Et J Fantini, N Yahi et C Di Scala vont déposer un projet européen en collaboration avec l'université d'Helsinki et l'université de Cambridge (Horizon 2030). L'obtention de ces fonds internationaux devrait nous permettre d'attirer encore davantage de doctorants et postdoctorants.

Recommandations sur le critère d'évaluation 2 : attractivité

UNIS est **internationalement reconnue** pour **ses travaux et son expertise** dans le domaine de la **neurobiologie des canaux ioniques**. De plus, elle a été capable **d'attirer de nombreux jeunes chercheurs** de l'étranger avec un **bagage scientifique et technique de très haut niveau**. Néanmoins, une recommandation faite par le comité serait de développer plus la synergie avec des centres internationaux afin de participer à des consortiums Européens pour acquérir des fonds internationaux. Comme précédemment évoqué, une de nos priorités pendant le prochain contrat quinquennal sera de multiplier nos réponses aux appels d'offre internationaux (NIH, HFSP, etc...) et européens (ERC, EraNet, Marie Skłodowska-Curie, EMBO, etc...). En

¹ Les liens et contacts sont déjà en cours

particulier, nos nombreuses collaborations nationales (R Brette ; G Sandoz, Nice ; S Lévi, Paris ; F Wendling, Rennes; B Gasnier Paris, etc...), européennes (S Hallermann, Leipiz, Allemagne, JJ Garrido, Madrid, Espagne; A Hierlemann, Bâle, Suisse; Helsinki ; Cambridge ; etc...) et extra-européennes (S Stupp, Chicago, USA ; P Chauvel, Pittsburgh USA ; Y Li, Beijing Chine ; N Brunel, Duke USA ; F Barrantes, Buenos Aires Argentine ; A McKinney, Montreal Canada, etc...) nous permettront de former des consortiums de grande qualité afin de répondre aux appels à projet européens et internationaux.

Recommandations sur le critère d'évaluation 3 : production scientifique

La production scientifique d'UNIS a été jugée de **très grande qualité**, publiée dans des **journaux scientifiques de premier plan** (Brain, Sci Adv, PNAS, eLife, J Infect, etc...) et **très bien citée**. Par conséquent, aucune recommandation n'a été faite.

Recommandations sur le critère d'évaluation 4 : contribution des activités de recherche vers la société

UNIS a développé de **nouvelles collaborations avec l'industrie et les hôpitaux**. De plus, les compétences d'UNIS en **modélisation moléculaire** et en biologie structurale ont conduit à des **partenariats importants avec l'industrie** et à la **création d'une start-up**. UNIS participe également à la **vulgarisation scientifique** au travers de sa participation financière et en personne à la Semaine du Cerveau. La recommandation du comité concerne l'extension de la contribution de l'UNIS vers la société au-delà de ce que nous faisons déjà. Nous envisageons plusieurs actions ciblées comme 1) notre participation à l'association Cerveau Point Comm, 2) des communications vers le grand public sur l'amblyopie (Dr A Aziz et Prof D Denis, journées d'ophtalmologie pédiatrique) et 3) des communications enregistrées (APHM TV). Par ailleurs, nous allons utiliser les réseaux sociaux pour communiquer sur notre recherche au plus grand nombre et nous rapprocher des services de communication AMU et INSERM afin d'étendre notre couverture de communication.

Vous souhaitant bonne réception des présentes,

Je vous prie de croire, Madame, Monsieur, l'expression de mes respectueuses salutations.

Eric BERTON



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